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RHEUMATOID ARTHRITIS

THE NATURAL HISTORY OF THE DISEASE AND ITS MANAGEMENT*

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RHEUMATOID arthritis is a capricious disease. The reason for its onset is hidden in mystery; its course depends on the whims of fancy. Its initiating cause has been attributed to trauma of bacterial, viral, protozoal, physical or psychic origin without unanimity of opinion. For our purposes tonight one must dismiss the pathogenesis as unknown. Volumes have been written concerning its management and the only agreement today concerning therapy rests on the use of common sense measures which your grandmother would have advised, such as rest, a good diet, salicylates, the prevention of deformities if at all possible, heat to sore areas, exercises to keep the patient limber, encouragement of the patient (the so-called optimistic attitude on the part of the physician), and retraining if damage cannot be or has not been prevented (rehabilitation).[1] These measures are uniformly accepted, in the writer's humble opinion, because they seldom do harm. Whether they are of any value is another question. No therapy requiring medical knowledge, wisdom or skill has received universal acceptance.

An oft-repeated adage states that therapy should be directed to-

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TABLE I—CLASSIFICATION OF END-RESULT AT TERMINATION OF FOLLOW-UP

Bed or chair ridden.
Deformities or flexion contractures and still complaining of joint pains, i.e., disease still active and may be progressing.
Deformities or flexion contractures and no complaints — commonly called burnt-out cases.
Occasional joint pains — without deformities or flexion contractures which interfere with existence.
No signs of arthritis.

wards modifying beneficially the natural history or course of a disease. By this latter term is meant the completely untreated disease, and in the present day such a test object is rarely found. However, if, in a large number of cases treated with various agents, the disease apparently follows a uniform course, such agents can be said to have influenced the disease little, if at all. In practically no instance have reports on therapy been evaluated in the light of the long-term natural history of the disease. In the past five years, two reports have appeared attempting to describe the natural history of the disease—one from the Massachusetts General Hospital[2] and one from our group.[3] It is difficult to appraise a disease such as rheumatoid arthritis, and in the report from MGH the status of the disease was classified as improved (with three categories of improvement), stationary or worse. We have tried to evolve a simple but admittedly arbitrary classification involving five categories—bed or wheelchair, flexion contractures or deformities and disease active, flexion contractures or deformities and disease inactive, minor joint complaints, and no arthritis, i.e., a complete remission (Table I).

It must be noted that this is a very arbitrary classification of end-results in a disease in which the will of the patient to do things and his ability to tolerate pain make such a great difference. True, the two categories at the extremes are beyond criticism since a patient confined to bed or wheelchair is a definite cripple from arthritis and a patient with no signs of arthritis can be considered cured in the limited sense of that word. However, in the three central categories, the personal equation enters a critical evaluation. We have patients with severe deformities and pain demonstrating all the criteria of Steinbrocker's Class IV[4] who are self-supporting and, amazingly, enjoying life. As the an-

TABLE II

Comparison of end-results in series at Massachusetts General Hospital[2] treated with conservative medical and orthopedic measures with series at Presbyterian Hospital[3] treated with many or no agents.

Massachusetts General Hospital Total cases — 250	*Per cent*		*Presbyterian Hospital* Total cases — 374	*Per cent*
Improved—Good end-result		53.2	Good end-result	48
in remission	15.2		no arthritis	26
moderately and slightly improved	38.0		occasional joint pains	22
Poor end-result		46.8	Poor end-result	52
stationary	12.8		flexion contractures and inactive	13
worse	34.0		flexion contractures and active	29
			bed or wheelchair	10

tithesis to this, we have patients with no deformities who after years of pain about the joints are true invalids in the sense that they spend their entire existence at the clinic and continue throughout the years to complain of their joint troubles. We have been unable to evaluate these factors on a statistical basis primarily because they are so elusive and subjective. However, it must be remembered that these very factors are those with which the patient is most concerned and towards which he feels therapy should be directed. A patient with a severe flexion contracture who chooses to ignore it is unimpressed with his bad end-result, whereas a patient with continuing joint pain without deformities whose whole life centers about his complaints cares little if he has no flexion contractures and fails to consider himself a "good end-result."

In the following discussion, these variables should be considered and all therapy must be regarded in their light, but from the objective viewpoint they cannot be included. Perhaps a large volume of patients will negate the isolated instances which make an objective interpretation of an end-result ridiculous. In summary, it may be said that the grouping used in our studies is arbitrary and leaves much to be desired but does have the advantage of objectivity and simplicity.

In the two studies, at Massachusetts General[2] and at Presbyterian,[3] there was considerable agreement as to the end-result in patients with rheumatoid arthritis taken at one point in time in that about 50 per cent did poorly (Table II). The indication for a severe prognosis in the

MGH study was typical symmetrical joint involvement. In our study the presence of a positive streptococcus agglutination test favored but did not indicate absolutely a poor end-result. Both the MGH group and ours stressed that the end-result was taken at one point in time since some of the patients apparently doing well at that particular time, if examined later, might fit into another category. It is important to stress the fluidity of this disease which waxes and wanes without obvious cause.

It would seem proper at this time to evaluate the accepted forms of therapy in the light of the natural history of the disease, if this is possible, and thereby determine which therapy has modified the disease beneficially.

Measures of so-called "proved" value[1] directed towards improving the patient's general health include: 1) *Rest* for the body as a whole and for the inflamed joints, both to be regulated carefully and combined with exercise as tolerated; 2) a nutritious, well-balanced and appetizing diet and general hygienic measures; 3) salicylates as antirheumatic and analgesic drugs and codeine for brief periods of time, if necessary; 4) prevention and correction of deformities; 5) physical and occupational therapy; 6) psychotherapy; and 7) rehabilitation. These measures were all employed in the study mentioned from the MGH. Their end-result in the group was roughly similar to ours in which some patients received all these measures, many received a few and some none. Thus, as a group, these measures failed to modify the end-result of the disease. It must again be stressed that for statistical purposes small degrees of improvement which would be of great importance to the patient are not shown in these data. No one would advocate the abandonment of these procedures since in most instances they can do no harm; furthermore, they may bring solace and temporary comfort to the patient, if not objective improvement. However, I do wish to stress that if harm does ensue from such procedures, their use may not be warranted. As an example of such harm, prolonged bed rest, even combined with careful supervision and regulated exercises, may be harmful to an individual with financial and family responsibilities which must be laid aside during such a stay in bed. Also, correction of deformities by operative orthopedic means leading to a joint in good position but firmly ankylosed may be of questionably beneficial value to the patient. Even if these measures did partially modify the course

of the disease, their absolute worth is open to considerable question since in individual cases, familiar to everyone who has handled a patient with rheumatoid arthritis, flexion contractures have developed and progressed during rest in bed with the joints splinted part of the day while the patient was on full doses of salicylate, receiving heat to the joint, muscle-setting exercises, and under the care of a competent psychiatrist. *Some* beneficial results may be expected from these measures of proven value in *some* cases, but since we are dealing with a disease requiring statistical evaluation of therapy, a comparison of the series from the MGH with ours leaves one with the impression that these measures of proven value have not modified the disease.

Rehabilitation—the training of a crippled patient to make the greatest use of his limited capacities is an extremely important phase of this problem since in so many instances prevention of crippling has not been attempted or has not been possible. Rehabilitation of the patient with rheumatoid arthritis is still in its infancy and no adequate survey has been made of its feasibility. However, at this point I would like to interject a word of caution. The great advances in rehabilitation in the past ten to fifteen years have been made on clinical material notable for the static nature of the disability. Thus in patients with paraplegia after poliomyelitis and with cerebral palsy, the injury has been sustained and rehabilitation takes over in an organism in which the cause of the disability itself is past. In such individuals, a steady progression of re-education is possible. In rheumatoid arthritis, one is dealing with a dynamic pattern in which new disabilities continue to occur while re-education of the static disabilities is being attempted. This makes for difficult rehabilitation and, at present, no certain answer can be given to the question, "is it possible by vigorous rehabilitory measures to re-educate a person crippled with rheumatoid arthritis to a sufficient degree to warrant the expenditure of time by the patient and the agencies involved?"

The place of psychotherapy in the treatment of rheumatoid arthritis is not clear. In a few scattered instances excellent therapeutic results have been reported following standard methods of psychotherapy. However, in a disease with such an unpredictable course, a large series of studies is necessary before one may reach a definite conclusion. One needs only a nodding acquaintance with the literature to realize that many measures have been advocated enthusiastically at first for the con-

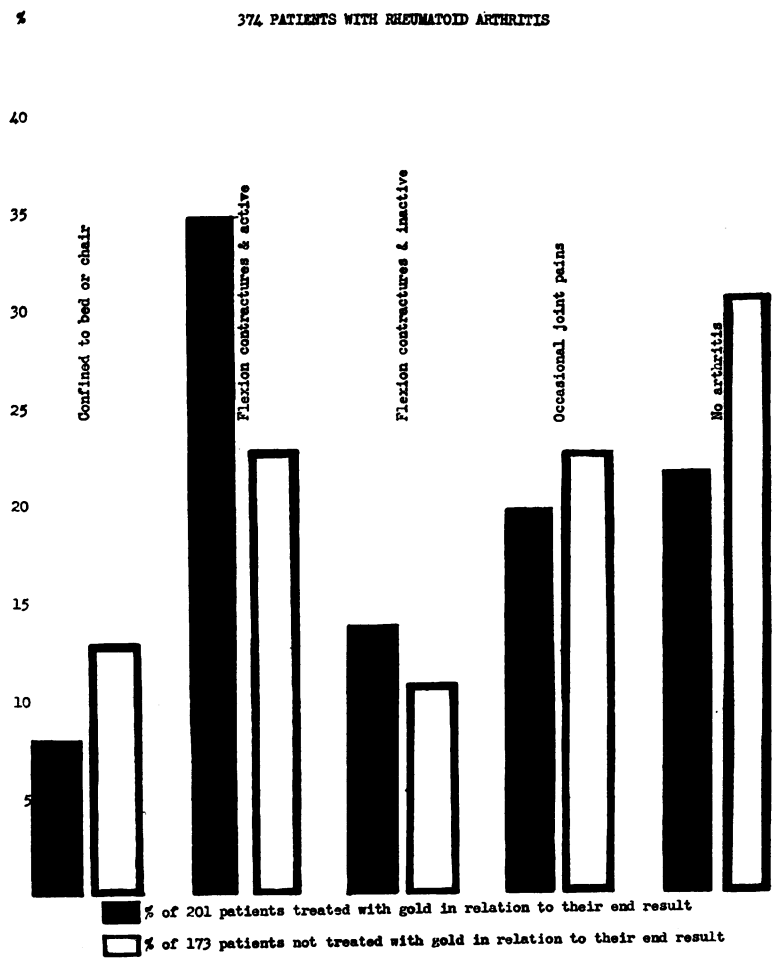

Fig. 1—Result at end of 5 years of patients with rheumatoid arthritis treated with more than 500 mgm. of gold compound compared with controls who received no chrysotherapy.

trol of rheumatoid arthritis only to be relegated to the scrapbasket after shorter or longer periods of time. Among certain groups working on the problem, the psychotherapeutic approach is now receiving considerable attention. With time one may be able to place this among the measures of proven value or throw it on the large pile labelled measures of no value.

Chrysotherapy or the use of gold compounds has been included under measures on which there is fairly uniform agreement but not complete unanimity. The treatment of rheumatoid arthritis with gold

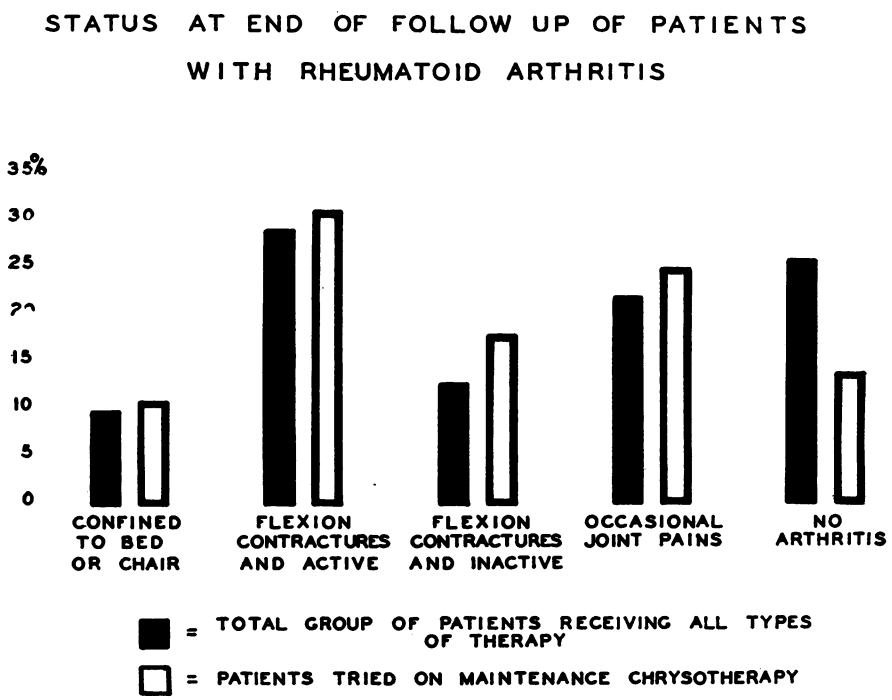

Fig. 2—Result at end of 5 years of 123 patients in whom maintenance gold therapy was attempted compared to the series as a whole.

compounds has been widely used in Europe for over fifteen years and in this country for ten. It has been described as "the one agent which has been shown to change the course of rheumatoid arthritis in a significant number of patients."[5]

In most instances this statement has been based on a group of patients followed at the most for one to two years following the administration of gold. In our experience, a remission induced by a course of gold is followed, when the gold is discontinued, sooner or later by a relapse.[6] We are of the opinion that gold does influence the course of the disease in a percentage of patients greater than would be expected in a similar group receiving no gold. However, in a limited number of patients in our group, we have been unable to convince ourselves that the administration of gold has changed the natural history of the disease when viewed from the perspective of the five-year follow-up (Fig. 1). Since a relapse of the disease of greater or lesser severity is likely to occur after the gold has been stopped, most people have advocated the

maintenance schedule of administration whereby gold is continued indefinitely and we ourselves have held out hopes for such a possibility. Recently we have reviewed our results with the maintenance gold schedule and have again been disheartened. We have followed 123 patients for an average of eight years, who have received gold over an average of a five-year period, receiving an average of 3.3 grams of gold compound. One of these patients received gold constantly. In the remainder the gold was stopped for various reasons—in the majority of instances because of toxicity or because of the failure of the patient to return to the clinic. The end-result has been identical with our total group of patients who received various therapeutic measures (Fig. 2). It should be noted that 20 per cent of these patients developed flexion contractures during the period of observation. These results are similar to those seen in syphilis treated with arsenicals where toxic reactions and the unwillingness of the patient to continue a protracted and tedious course of treatment occasionally interfered with a good therapeutic result.

It is worthwhile mentioning at this point that the optimistic statement quoted above about gold in our opinion still holds true but the difficulty rests in our inability to continue a gold-induced remission indefinitely or even for the prescribed five-year period in a significant number of patients. Advocates of chrysotherapy suggest that the best results occur when gold is started in the first year of the disease. In our opinion, in the absence of a positive streptococcus agglutination or definite x-ray changes, the certain diagnosis of rheumatoid arthritis is difficult in the first year of the disease. The recent report of Adams and Cecil[7] on the use of gold in such a group of patients well-controlled by a group receiving no gold leaves little doubt that, in this group of early cases, chrysotherapy is of definite value. The only cavil we have with this view is that the result is of temporary value when viewed from the standpoint of a chronic disease where the standard five-year follow-up is but a pause in the long dreary years of disease. We have a small group of patients seen in the first two years of their disease. These happily divided themselves almost equally into those who had received gold and those who had not. In the "five years and over" follow-up study (Fig. 3), no difference was apparent between the two groups.

The value of chrysotherapy in the treatment of rheumatoid arthritis seems to rest on its temporary effect which in our minds is beneficial.

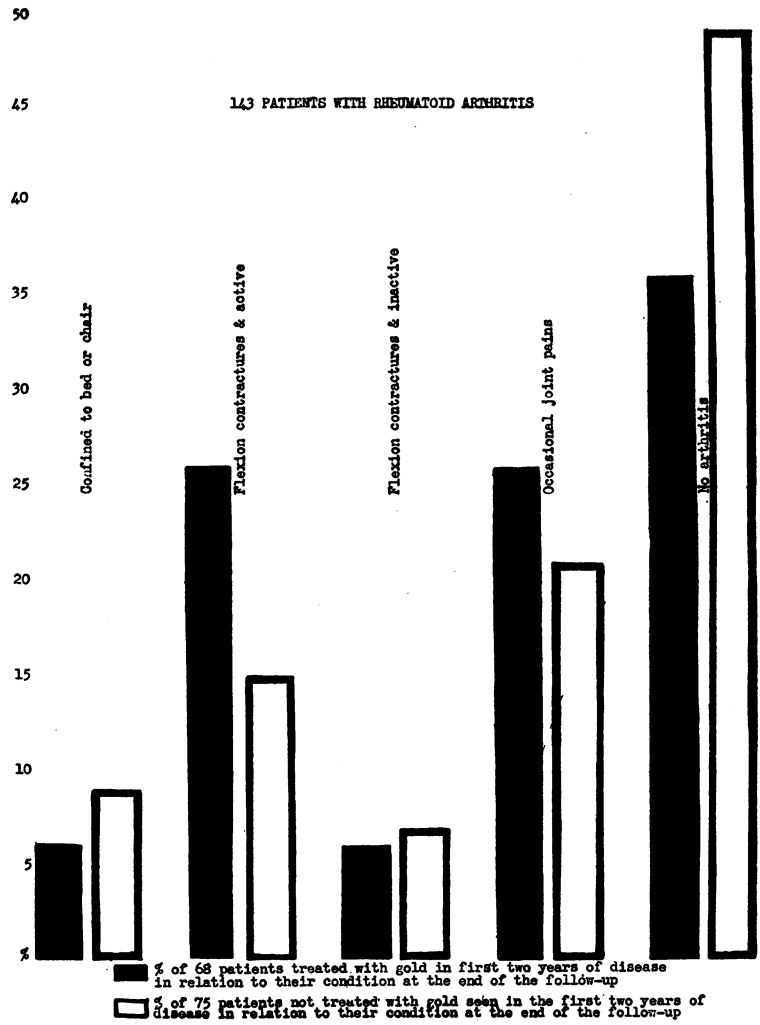

Fig. 3—Result at end of 5 years of 143 patients with rheumatoid arthritis seen in the first two years of their disease. Sixty-eight were treated with gold within two years of onset of disease (63% good end-result); 75 received no gold (70% good end-result).

With continued use the physician is frequently unable to continue this benefit and the patient again resumes the natural course uninfluenced by the gold. It is a philosophical question which I am not prepared to answer, whether the use of gold is warranted since its usefulness is of a temporary nature and there are real dangers—at present seldom lethal —attendant upon its use.

Two other measures are mentioned upon which there is fairly uni-

form but not complete agreement. The first is the use of multiple transfusions. There has been no serious volume study of this agent which would indicate its value. Favorable reports have not included a large series of cases or an adequate period of observation. Numerous individual results which have not seemed to modify the disease have been observed by physicians caring for patients with rheumatoid arthritis. The expense, the brief duration of benefit and the danger of homologous serum jaundice would seem to mitigate against the use of this form of therapy in many patients with rheumatoid arthritis.

The second suggestion in this category is a move to an equable climate. In this field there is no unanimity of opinion and no study including a large number of cases upon which to base an opinion. We have seen patients with rheumatoid arthritis who moved from the eastern seaboard to the south, southwest, or far west, and a remission has ensued following the move. We have also seen the converse. Suffice it to say that the treatment of rheumatoid arthritis in these areas is identical with treatment advocated in the cold and exceedingly unequable climate of the northeast. Since the disease is said to appear only rarely in natives of tropical countries in their native habitat, there is a possibility that the temperate climate may have some bearing on the disease. Since the number of variables which exist between a temperate and a tropical pattern of life is greater than the temperature and the humidity, the exact relationship between climate and rheumatoid arthritis is difficult to define. In the management of a patient with rheumatoid arthritis, advice as to a move to another climate should be given only after many points in the individual patient's way of life have been considered. A move not financially feasible is not justified; a move away from a closely-knit family group leading to great loneliness is often inadvisable; a move to an area in which medical care is inadequate should be discouraged. As in the management of any chronic disease, the personal factors in a person's life situation should receive a great deal of attention when one considers taking positive action which cannot be considered absolutely essential to the care of the disease.

The picture given above of the management of the patient with rheumatoid arthritis is not a cheerful one since, from our observation in a group of cases chosen from a clinic practice, we have not been able to convince ourselves of the certain value of any form of therapy in modifying the untreated course of the disease. Perhaps in a private

practice such a discouraging outlook is not warranted since freedom from the fear of financial insecurity may not play so great a role in changing the accepted forms of therapy. Perhaps a physician with a more personal relation with the patient than that permitted in the clinic can achieve a maintenance form of gold therapy in a large group of patients. We have not been able to do this and are forced to admit that all our therapy has not to date modified the disease. As emphasized earlier, these data have been derived from objective evidence and the subjective complaints of a patient with rheumatoid arthritis have not been considered. These are undoubtedly helped by any or all of the measures outlined above. These patients feel better when an interest is shown in their progress and unquestionably are helped by loving care.

A more cheerful note might be interjected at this point. Dr. Bunim[8] has described the effects of cortisone and ACTH on rheumatoid arthritis and the effect of these hormones certainly leaves no doubt in the mind of anyone as to their efficacy in controlling the symptoms of this disease. True, at this time only a year and a half after the dramatic announcement of Hench, Kendall and their associates,[9] it is impossible to evaluate their effect upon its natural history. Certain portents can, however, be seen. As we have stressed time and again, deformities—chiefly flexion contractures—are the major problem in rheumatoid arthritis. If treated early with ACTH or cortisone—usually within six months—these can be controlled. It is possible that the control of deformities can be achieved by other than continuous administration of the hormones. Previous to the use of induced hyperadrenalism, physical therapy—chiefly active and passive exercises—in the patient with rheumatoid arthritis was restricted to the limits of pain and fatigue. If these limits were exceeded, the results were usually disastrous in that the patient was so disabled the following day, no further exercises could be undertaken. The uselessness of any such plan of muscle building should be familiar to any one who has gone through a program of athletic training. To achieve an increase in muscle strength, muscles must be overworked and when limits to this amount of work are set, very little new muscle power is achieved. Dr. James Coss[10] of our group has noted that when a patient is on cortisone and ACTH, exercises can be carried beyond the limits of pain and fatigue without complete disability the following day. In this fashion, the patient with rheumatoid arthritis while under the influence of cortisone and ACTH may be

treated as a normal individual and exercises can be carried forward as in the usual conditioning program. This is of great value in the rehabilitation of the patient and may portend a new era in rehabilitation as applied to rheumatoid arthritis.

Lastly, there is some hope that orthopedic surgery can be combined with cortisone given parenterally and also locally into the operated joint.[11] In this way, it is hoped that the incidence of ankylosis due to the development of fibrous adhesions postoperatively may be decreased.

In summary, one may say that the management of the patient with rheumatoid arthritis depends in large part on plain common sense. The patient must be considered as an individual in addition to a collection of sore joints. In our experience nothing in the past has modified the natural course of the disease during which about half the patients recover regardless of therapy and about a sixth do very badly. With the introduction of ACTH and cortisone, much encouragement can be given to the 50 per cent who do not recover and particularly to those unfortunates in the 15 per cent who formerly did very badly. There is also hope that the patients who comprised this group in the past may be rehabilitated to a certain extent by the use of all the measures outlined above in conjunction with the use of ACTH or cortisone. Although sufficient time has not passed since the introduction of these hormones in the treatment of rheumatoid arthritis to state that their use will modify the natural history of the disease, the signs are definitely encouraging.

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